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PubMed Nucleotide Protein Genome Structure PMC Taxonomy OMIM

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***138945**

Links

GRANULIN; GRN***Alternative titles; symbols*****PROGRANULIN**Gene map locus [17q21.32](#)**TEXT**

The granulins are a family of cysteine-rich polypeptides, some of which have growth modulatory activity. The widespread occurrence of granulin mRNA in cells from the hematopoietic system and in epithelia implies important functions in these tissues. All 4 known human granulin-like peptides are encoded in a single precursor, progranulin, which has a highly conserved 12-cysteine backbone defining a consensus sequence that is repeated 7 times ([Bhandari et al., 1992](#)). Using DNA from human-hamster somatic cell hybrids, [Bhandari and Bateman \(1992\)](#) assigned the granulin precursor gene to chromosome 17. A protein-coding region of the gene was shown to comprise 12 exons covering about 3,700 bp. Each tandem granulin repeat is encoded by 2 nonequivalent exons, a configuration unique to the granulins that would permit the formation of hybrid granulin-like proteins by alternate splicing. 

Progranulin is a 593-amino acid glycoprotein, the mRNA of which is expressed in many epithelial cells both in vitro and in vivo. [He and Bateman \(1999\)](#) demonstrated that overexpression of the progranulin gene in SW-13 adrenal carcinoma cells and MDCK nontransformed renal epithelia resulted in transfection-specific secretion of progranulin, acquired clonogenicity in semisolid agar, and increased mitosis in monolayer culture, whereas diminution of progranulin gene expression impaired growth of these cells. They proposed that the rate of growth of some epithelia is proportional to the level of intrinsic progranulin gene expression, and that elevated progranulin gene expression confers a transformed phenotype on epithelial cells including anchorage independence in vitro and growth as tumors in nude mice. 

In the course of studying the relationship between the ITGA2B ([173470](#)) and ITG3B ([273800](#)) genes, which are both located on 17q21.32, [Thornton et al. \(1999\)](#) found that the GRN gene is located approximately 18 kb downstream to ITGA2B.

Liau et al. (2000) found that the 2.1-kb granulin mRNA is expressed predominantly in glial tumors of the brain, with lower levels in spleen, kidney, and testis, whereas expression was not detected in nontumor brain tissues. The differential expression pattern, tissue distribution, and implication of this glioma-associated molecule in growth regulation suggested a potentially important role for granulin in the pathogenesis and/or malignant progression of primary brain neoplasms. 🧠

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Structure and chromosomal location of the human granulin gene. *Biochem. Biophys. Res. Commun.* 188: 57-63, 1992.
PubMed ID : [1417868](#)
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Isolation and sequence of the granulin precursor cDNA from human bone marrow reveals tandem cysteine-rich granulin domains. *Proc. Nat. Acad. Sci.* 89: 1715-1719, 1992.
PubMed ID : [1542665](#)
3. He, Z.; Bateman, A. :
Progranulin gene expression regulates epithelial cell growth and promotes tumor growth in vivo. *Cancer Res.* 59: 3222-3229, 1999.
PubMed ID : [10397269](#)
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Identification of a human glioma-associated growth factor gene, granulin, using differential immuno-absorption. *Cancer Res.* 60: 1353-1360, 2000.
PubMed ID : [10728698](#)
5. Thornton, M. A.; Poncz, M.; Korostishevsky, M.; Yakobson, E.; Usher, S.; Seligsohn, U.; Peretz, H. :
The human platelet alpha-IIb gene is not closely linked to its integrin partner beta-3. *Blood* 94: 2039-2047, 1999.
PubMed ID : [10477733](#)

CONTRIBUTORS

Victor A. McKusick - updated : 5/1/2000
Victor A. McKusick - updated : 1/6/2000
Victor A. McKusick - updated : 9/15/1999

CREATION DATE

Victor A. McKusick : 11/24/1992

EDIT HISTORY

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mgross : 9/16/1999
terry : 9/15/1999
carol : 2/11/1993
carol : 1/25/1993
carol : 11/24/1992

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SEARCH REQUEST FORM

58431

Requestor's Name: Natalie Davis Serial Number: 09/880842
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Search Topic:

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Please search for a method of determining
 tumorigenicity + determining if a patient is
 resistant to anti-neoplastic effects of antiestrogen
 therapy by determining the number of GPR8
 positive cells in a sample from a patient.

Key claims: 1, 27, 28, 64 + 65

1/16/02
 11:16
 1/16/02

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Date completed: <u>1/25/02</u>	Search Site	Vendors
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Elapsed time: <u>23</u>	<input type="checkbox"/> Pre-S	<input checked="" type="checkbox"/> Dialog <u>76.42</u>
CPU time: _____	Type of Search	<input type="checkbox"/> APS
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File 155:MEDLINE(R) 1966-2002/JAN W3

File 5:Biosis Previews(R) 1969-2002/Jan W3
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File 315:ChemEng & Biotec Abs 1970-2002/Dec
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File 73:EMBASE 1974-2002/Jan W3
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File 399:CA SEARCH(R) 1967-2002/UD=13604
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File 351:Derwent WPI 1963-2001/UD,UM &UP=200206
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?ds

Set	Items	Description
S1	73	GP88 OR GP()88
S2	4064058	CANCER? OR TUMOR? OR TUMOUR? OR CARCINO? OR NEOPLAS?
S3	20710	ANTIESTROGEN? OR ANTI()ESTROGEN?
S4	441004	BREAST? ?
S5	39186	TAMOXIFEN
S6	11	S1 AND S2
S7	0	S1 AND S3
S8	276294	ESTROGEN?
S9	0	S1 AND S8
S10	4	S4 AND S1
S11	0	S5 AND S1
S12	6	S1 AND DIAGNOS?
S13	12	S1 AND (SENSITIV? OR RESIST?)
S14	6	S13 NOT (VIRUS OR VIRAL)
S15	18	S6 OR S10 OR S12 OR S14
S16	10	RD S15 (unique items)

?t 16/7/all

16/7/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10757256 99088715 PMID: 9871549

Synthesis and pharmacological activity of the stereoisomers of GP - 88 ,
a propafenone-type modulator of multidrug resistance .

Chiba P; Rebitzer S; Richter E; Hitzler M; Ecker G
Institute of Pharmaceutical Chemistry, University of Vienna, Wien,
Austria.

Bioorganic & medicinal chemistry letters (ENGLAND) Apr 7 1998, 8 (7)
p829-32, ISSN 0960-894X Journal Code: C8B

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

All four stereoisomers of the propafenone-type MDR-modulator GP - 88
(1) were synthesized using a combined approach with chiral pool building
blocks and an acetalic protective group, which allows not only
diastereoseparation but also assignment of absolute configuration via NMR
spectroscopy. Those isomers with different configuration on the center of
chirality in the propanolamine side chain showed statistically different
PGP-inhibitory activity. Generally, the (R)-configured isomers were by a
factor of nearly two higher active than the (S)-isomers. No differences in
activity were observed for isomers with different configuration on the
benzylic center of chirality.

Record Date Created: 19990127

16/7/2 (Item 2 from file: 155)
DIALOG(R) File 155:MEDLINE(R)

05884774 86305080 PMID: 3745505

Biochemical characterization of the major peanut-agglutinin-binding glycoproteins in vertebrate retinae.

Hageman GS; Johnson LV

Journal of comparative neurology (UNITED STATES) Jul 22 1986, 249 (4)
p499-510, 482-3, ISSN 0021-9967 Journal Code: HUV

Contract/Grant No.: EY04741, EY, NEI

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

Peanut agglutinin (PNA), a lectin that binds D-galactose-beta (1----3) N-acetyl-D-galactosamine disaccharide linkages, selectively labels cone photoreceptors in the retinae of a variety of species. PNA binds consistently to domains of the interphotoreceptor matrix associated with cone, but not rod, inner and outer segments, to cone cell body and axonal membranes, to cone synaptic pedicles, and to portions of the inner plexiform layer. In order to begin the characterization of the molecular species responsible for cone-specific PNA binding, chick, turkey, rat, dog, pig, monkey, and human retinal extracts were separated by SDS-polyacrylamide gel electrophoresis and probed with peroxidase-conjugated PNA. The results reveal the presence of six major groups of PNA-binding glycoproteins ranging from 30 to 88 kilodaltons. Most of these are shared by the seven species examined; however, some interspecies variation is present. Three groups, designated GP39/40, GP42/45, and GP60, are the most intensely labeled by PNA and are common to all species analyzed, while groups GP29/31 and GP88 are less intensely labeled and are present in most but not all of the species investigated. Labeling of the GP54 group is variable but is most consistently associated with extracts of rat and pig retinae. Trypsin treatment, which results in the loss of cone-associated PNA binding in the interphotoreceptor matrix, causes a visually detectable reduction in three of the six groups of PNA-binding glycoproteins in porcine retinal extracts. Of these, GP54 is the most sensitive, being undetectable on PNA-stained blots after only 5 minutes of enzyme exposure; GP88 and GP45 are less sensitive but both are markedly reduced after 15 minutes of trypsinization. Trypsin-sensitive molecules thus may be involved in the establishment of the cone-specific domains of interphotoreceptor matrix identified by PNA binding. These, as well as the other groups of PNA-binding molecules, are being utilized to develop more specific immunologic probes with which to further study of their distribution and function.

Record Date Created: 19860929

16/7/3 (Item 3 from file: 155)
DIALOG(R) File 155:MEDLINE(R)

05841870 87096145 PMID: 3799062

Antigenic variation among human strains of influenza C virus detected with monoclonal antibodies to gp88 glycoprotein.

Sugawara K; Nishimura H; Kitame F; Nakamura K

Virus research (NETHERLANDS) Oct 1986, 6 (1) p27-32, ISSN 0168-1702

Journal Code: X98

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

Antigenic variation among influenza C virus strains was investigated with monoclonal antibodies against gp88 glycoprotein. Seven monoclonal antibodies obtained were tentatively classified into two groups, A and B. The group A antibodies had hemagglutination inhibition (HI), hemolysis inhibition and neutralization activities whereas the group B antibodies possessed none of them. A comparison of antigenicity among 15 human strains with these antibodies in radioimmunoprecipitation and HI tests showed that the regions recognized by the group A antibodies undergo considerable changes, whereas those by group B are conserved among the strains.

Record Date Created: 19870217

16/7/4 (Item 4 from file: 155)

DIALOG(R) File 155:MEDLINE(R)

05815228 86241438 PMID: 2424405

The functions of oligosaccharide chains associated with influenza C viral glycoproteins. II. The role of carbohydrates in the antigenic properties of influenza C viral glycoproteins.

Hongo S; Sugawara K; Homma M; Nakamura K

Archives of virology (AUSTRIA) 1986, 89 (1-4) p189-201, ISSN 0304-8608 Journal Code: 8L7

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

The antigenic properties of influenza C viral glycoprotein gp88 were compared with those of its nonglycosylated counterpart T76 synthesized in infected cells treated with tunicamycin. Radioimmunoprecipitation experiments with three different monoclonal antibodies against gp88 revealed that an antibody designated Q-5 precipitated gp88 but not T76, indicating the requirement for glycosylation for the binding of this antibody to gp88. It is unlikely, however, that the antigenic determinant recognized by Q-5 is carbohydrate moiety since the ability of the antibody to bind to gp88 varied depending on the virus strain, and trypsin-treatment of gp88 eliminated its reactivity with Q-5. Gel electrophoretic analysis under nonreducing conditions showed that T76 underwent the formation of disulfide-linked multimers in the absence of reducing agent while gp88 behaved as monomers, suggesting that glycosylation is required for gp88 molecules to attain an appropriate conformation. These observations, altogether, suggests that glycosylation is important in determining the immunological specificity of gp88 presumably by influencing the folding of this glycoprotein.

Record Date Created: 19860701

16/7/5 (Item 5 from file: 155)

DIALOG(R) File 155:MEDLINE(R)

04769713 85042063 PMID: 6093357

Further characterization of proteins assembled by vesicular stomatitis virus from human tumor cells.

Zavada J; Huang AS

Virology (UNITED STATES) Oct 15 1984, 138 (1) p16-25, ISSN

0042-6822 Journal Code: XEA

Contract/Grant No.: AI-16625, AI, NIAID; AI-20896, AI, NIAID

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

Vesicular stomatitis virus (VSV), when reproduced in human tumor cell lines, assembled a specific subset of cell-derived proteins. These were detected by ³⁵S]methionine labeling of cells prior to infection and subsequent immunoprecipitation of VSV grown in these cells, as well as by direct immunoprecipitation of labeled cell extracts with antiserum directed against the VSV-assembled proteins. Their molecular weight (Mr) ranged between 15K and 180K; the larger proteins were glycosylated. Two of the major protein species (gp88 and gp130) were common to all four cell lines used (HeLa-cervical carcinoma, T47D- breast carcinoma, and HMB2 and SK1477-two melanoma cell lines). Proteins of other molecular weights were detected only in one or two of the cell lines. The melanoma cell lines (even in the absence of VSV) shed large particulate material which had contained the same spectrum of proteins that were assembled by VSV. The major protein component had an Mr of 30K. Some of the VSV-assembled proteins might possibly serve as specific tumor markers. It is also conceivable that the proteins assembled by VSV as well as the large particulate material might be products of defective endogenous human retroviruses.

Record Date Created: 19841123

16/7/6 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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13378191 BIOSIS NO.: 200200007012
88kDa tumorigenic growth factor and antagonists.
AUTHOR: Serrero Ginette(a)
AUTHOR ADDRESS: (a)10200 Savoy Ct., Ellicott City, MD, 21042**USA
JOURNAL: Official Gazette of the United States Patent and Trademark Office
Patents 1251 (5):pNo Pagination Oct. 30, 2001
MEDIUM: e-file
ISSN: 0098-1133
DOCUMENT TYPE: Patent
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: This invention relates to products and methods for treating cancer and for diagnosing tumorigenicity and other diseases associated with alteration in GP88 expression or action. Antagonists to an 88 KDa autocrine growth and tumorigenicity stimulator are provided which inhibit its expression or biological activity. The antagonists include antisense oligonucleotides and antibodies.

16/7/7 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE
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03597614 EMBASE No: 1988047050

Distribution of the antibody to influenza C virus in dogs and pigs in Yamagata prefecture, Japan

Ohwada K.; Kitame F.; Sugawara K.; Nishimura H.; Homma M.; Nakamura K.
Laboratory Animal Center, Department of Bacteriology, Yamagata University
School of Medicine, Yamagata 990-23 Japan
Microbiology and Immunology (MICROBIOL. IMMUNOL.) (Japan) 1987, 31/12
(1173-1180)
CODEN: MIIMD ISSN: 0385-5600
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

The distribution of the antibody to influenza C virus in the dogs and pigs in Yamagata prefecture, Japan was investigated by using three different serological methods: hemagglutination-inhibition (HI), radioimmunoprecipitation (RIP), and immunoblotting. The antibody against influenza C virus glycoprotein (gp88) was detected in 5 out of 112 sera collected from mongrel dogs, three by RIP test and two by any of the three methods, suggesting that the virus can cause natural infection in dogs. significant levels of HI activity were found in 58 out of 269 sera collected from domestic pigs, but none of them showed positive reaction in the more sensitive method RIP, which suggests that the inhibitors against the hemagglutination by influenza C virus rather than the antibody to gp88 are responsible for the observed HI activity. It appears, therefore, that at least in the Yamagata area, pigs do not play significant roles in the spread of influenza C virus in humans.

16/7/8 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE
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01702261 EMBASE No: 1980070507

The synthesis of glycoproteins in human melanoma cells infected with varicella-zoster virus

Grose C.
Virol. Lab., Dept. Ped., Univ. Texas Hlth Sci. Cent., San Antonio, Tex.
78284 United States
Virology (VIROLOGY) (United States) 1980, 101/1 (1-9)
CODEN: VIRLA
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH

The synthesis of glycoproteins has been investigated in cultured human melanoma cells before and after infection with varicella-zoster virus (VZV). The glycosylated polypeptides were labeled with tritiated precursors of the sugar moiety and were analyzed by polyacrylamide gel electrophoresis. When the electrophoretic profiles of uninfected and infected cell lysates were compared, a marked reduction in host cell glycoprotein synthesis was evident during the late phase of viral infection. In addition, at least three infected-cell specific (ICS) glycosylated polypeptides were detected. After immune precipitation of (sup 3H)glucosamine-labeled VZV cell extracts with human and rabbit VZV antisera, a total of 5 ICS glycoproteins were identified and designated gp 45, gp 62, gp 88, gp 98, and gp 118, according to their apparent molecular weights (X10sup 3). Four of the 5 polypeptides (but not gp 88) were visualized after immune precipitation of infected cell extracts labeled with (sup 3H)fucose. The ICS glycopeptides corresponded in molecular weight to (sup 3sup 5S)methionine-labeled polypeptides detected in a virus-enriched fraction obtained by centrifugation of sonically

disrupted infected cells in a combination density-viscosity gradient. A prominent ICS high-molecular weight (~150,000) nonglycosylated polypeptide was identified also in the latter fraction.

16/7/9 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
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135340241 CA: 135(24)340241x PATENT
Human 88-KDa tumorigenic growth factor and its antagonists for cancer
diagnosis and therapy
INVENTOR(AUTHOR): Serrero, Ginette
LOCATION: USA
PATENT: United States ; US 6309826 B1 DATE: 20011030
APPLICATION: US 991862 (19971216) *US 863079 (19970523)
PAGES: 52 pp., Cont.-in-part of U.S. Ser. No. 863,079, abandoned.
CODEN: USXXAM LANGUAGE: English CLASS: 435006000; C12Q-001/68A;
C12P-019/34B; C12N-015/11B; C07H-021/04B
SECTION:
CA203003 Biochemical Genetics
CA201XXX Pharmacology
CA202XXX Mammalian Hormones
CA213XXX Mammalian Biochemistry
CA214XXX Mammalian Pathological Biochemistry
CA263XXX Pharmaceuticals
IDENTIFIERS: tumorigenic growth factor glycoprotein GP88 cDNA sequence
human, antibody antisense oligonucleotide antitumor drug glycoprotein GP88
antagonists
DESCRIPTORS:
Antitumor agents...
adipose tissue, GP88 antagonists as; 88-KDa tumorigenic growth factor
and antagonists
Hybridoma...
anti-GP88 antibody-producing; 88-KDa tumorigenic growth factor and
antagonists
Growth factors, animal...
autocrine, GP88 as; 88-KDa tumorigenic growth factor and antagonists
Antitumor agents...
brain, GP88 antagonists as; 88-KDa tumorigenic growth factor and
antagonists
Diagnosis...
cancer; 88-KDa tumorigenic growth factor and antagonists
Animal cell line...
C57MG, GP88 mRNA overexpression in; 88-KDa tumorigenic growth factor
and antagonists
Receptors...
for glycoprotein GP88; 88-KDa tumorigenic growth factor and antagonists
Gene, animal...
for GP88, of human; 88-KDa tumorigenic growth factor and antagonists
Enzymes, biological studies... Fluorescent dyes... Isotopomers...
Radionuclides...
for probe labeling; 88-KDa tumorigenic growth factor and antagonists
Northern blot hybridization...
GP88 mRNA detection assay; 88-KDa tumorigenic growth factor and
antagonists
Adipose tissue, neoplasm... Animal tissue... Brain, neoplasm...

Kidney,neoplasm... Liver,neoplasm... Ovary,neoplasm... Testis,neoplasm...
GP88 mRNA distribution pattern in; 88-KDa tumorigenic growth factor and
antagonists

Glycoproteins,specific or class...
GP88, of human; 88-KDa tumorigenic growth factor and antagonists

Antitumor agents...
hepatoma, GP88 antagonists as; 88-KDa tumorigenic growth factor and
antagonists

Liver,neoplasm...
hepatoma, inhibitors, GP88 antagonists as; 88-KDa tumorigenic growth
factor and antagonists

Brain,neoplasm... Kidney,neoplasm... Ovary,neoplasm... Testis,neoplasm...
inhibitors, GP88 antagonists as; 88-KDa tumorigenic growth factor and
antagonists

Antitumor agents...
kidney, GP88 antagonists as; 88-KDa tumorigenic growth factor and
antagonists

Antitumor agents...
mammary gland, GP88 antagonists as; 88-KDa tumorigenic growth factor
and antagonists

Animal cell line...
MCF-7, GP88 mRNA overexpression in; 88-KDa tumorigenic growth factor
and antagonists

Animal cell line...
MDA-MB-453, GP88 mRNA overexpression in; 88-KDa tumorigenic growth
factor and antagonists

Animal cell line...
MDA-MB-468, GP88 mRNA overexpression in; 88-KDa tumorigenic growth
factor and antagonists

Animal cell line...
MDA-468, GP88 protein overexpression in; 88-KDa tumorigenic growth
factor and antagonists

Mammary gland...
neoplasm, GP88 mRNA distribution pattern in; 88-KDa tumorigenic growth
factor and antagonists

Mammary gland...
neoplasm, inhibitors, GP88 antagonists as; 88-KDa tumorigenic growth
factor and antagonists

Antibodies...
neutralizing, GP88-binding; 88-KDa tumorigenic growth factor and
antagonists

Molecular association...
of glycoprotein GP88 and its cell surface receptor; 88-KDa tumorigenic
growth factor and antagonists

Iodination...
of GP88; 88-KDa tumorigenic growth factor and antagonists

Antitumor agents...
ovary, GP88 antagonists as; 88-KDa tumorigenic growth factor and
antagonists

Animal cell line...
PC, GP88 mRNA overexpression in; 88-KDa tumorigenic growth factor and
antagonists

Animal tissue...
peripheral, GP88 mRNA distribution pattern in; 88-KDa tumorigenic
growth factor and antagonists

Nucleic acid hybridization...
RNA protection assay, GP88 mRNA detection assay; 88-KDa tumorigenic

growth factor and antagonists
 PCR(polymerase chain reaction)...
 RT-PCR (reverse transcription-PCR), GP88 mRNA detection assay; 88-KDa
 tumorigenic growth factor and antagonists
 Antitumor agents...
 testis, GP88 antagonists as; 88-KDa tumorigenic growth factor and
 antagonists
 Antisense DNA... Antisense oligonucleotides... cDNA sequences... Genetic
 vectors... Molecular cloning... Probes(nucleic acid)... Protein sequences
 ... Transformation,genetic...
 88-KDa tumorigenic growth factor and antagonists
 CAS REGISTRY NUMBERS:
 147036-84-8 216663-36-4P amino acid sequence; 88-KDa tumorigenic growth
 factor and antagonists
 14158-31-7 biological studies, for GP88 labeling; 88-KDa tumorigenic
 growth factor and antagonists
 140086-63-1 216663-35-3P nucleotide sequence; 88-KDa tumorigenic growth
 factor and antagonists
 371180-05-1 371180-06-2 371180-07-3 371180-08-4 371180-09-5
 371180-10-8 371180-11-9 unclaimed nucleotide sequence; human 88-KDa
 tumorigenic growth factor and its antagonists for cancer diagnosis and
 therapy
 371112-48-0 371112-49-1 371112-50-4 371112-51-5 371112-52-6 unclaimed
 sequence; human 88-KDa tumorigenic growth factor and its antagonists
 for cancer diagnosis and therapy

16/7/10 (Item 1 from file: 351)
 DIALOG(R) File 351:Derwent WPI
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012239168

WPI Acc No: 1999-045276/199904

Composition containing antagonist of growth factor GP88 - useful for
 treating cancer and viral diseases and also for diagnosing disease
 from altered GP88 expression

Patent Assignee: SERRERO G (SERR-I)

Inventor: SERRERO G

Number of Countries: 083 Number of Patents: 004

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
WO 9852607	A1	19981126	WO 98US10555	A	19980522	199904 B
AU 9877978	A	19981211	AU 9877978	A	19980522	199917
EP 1011723	A1	20000628	EP 98926056	A	19980522	200035
			WO 98US10555	A	19980522	
US 6309826	B1	20011030	US 97863079	A	19970523	200172
			US 97991862	A	19971216	
			US 97991862	A	19971216	

Priority Applications (No Type Date): US 97991862 A 19971216; US 97863079 A
 19970523

Patent Details:

Patent No Kind Lan Pg Main IPC Filing Notes

WO 9852607 A1 E 96 A61K-039/395

Designated States (National): AL AM AT AU AZ BA BB BG BR BY CA CH CN CU
 CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR
 LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM

TR TT UA UG UZ VN YU ZW

Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR
IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW

AU 9877978 A A61K-039/395 Based on patent WO 9852607

EP 1011723 A1 E A61K-039/395 Based on patent WO 9852607

Designated States (Regional): AL AT BE CH CY DE DK ES FI FR GB GR IE IT
LI LT LU LV MC MK NL PT RO SE SI

US 6309826 B1 C12Q-001/68 CIP of application US 97863079
Cont of application US 97991862

Abstract (Basic): WO 9852607 A

Composition contains an antagonist (I) of GP88 (an 88 kDa glycoprotein growth factor). Also new are: (1) expression vectors containing cDNA (II) that encodes GP88 ; (2) diagnosis of tumorigenicity by measuring an elevated level of GP88 in tissue (relative to that in normal or peripheral tissue), and (3) diagnosing diseases associated with alterations in GP88 activity by measuring: (i) GP88 binding to cell surface receptors, or (ii) expression of these receptors.

USE - (I) are used to treat diseases associated with increased expression of GP88 , particularly cancer but also viral infections. Fragments of GP88 are used to raise specific antibodies (used as (I), as diagnostic reagents and for delivering toxins or other compounds to GP88 -expressing cells) and to screen for antibodies. Methods (2) and (3) are used to diagnose cancer , to determine susceptibility to GP88 -related disease and/or to therapy with (I), also to assess severity of disease. GP88 , an epithelin/granulin precursor, is a growth factor, particularly an autocrine factor for cells that produce it. It is tightly regulated in normal cells but unregulated (overexpressed) in highly tumorigenic cells.

Dwg.0/15

Derwent Class: B04; D16

International Patent Class (Main): A61K-039/395; C12Q-001/68

International Patent Class (Additional): A01N-043/04; A61K-031/70;

C07H-021/04; C12N-015/11; C12P-019/34

?logoff hold



MIM *138945

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[References](#)

[Contributors](#)

[Creation Date](#)

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[Gene map](#)

[LocusLink](#)

[Nomenclature](#)

[RefSeq](#)

[GenBank](#)

[Protein](#)

[UniGene](#)

[LinkOut](#)

Set	Items	Description
S1	32	PCDGF
S2	344	GRANULIN
S3	79	GRANULIN (W) PRECURSOR
S4	11	EPITHELIN PRECURSOR
S5	4345913	TUMOR? OR CANCER? OR NEOPLA?
S6	41	(S1 OR S3 OR S4) AND S5
S7	34	S6 NOT PY=>2002
S8	15	RD (unique items)

8/9/1 (Item 1 from file: 5)

DIALOG(R)File 5: Biosis Previews(R)

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13648129 BIOSIS NO.: 200200276950

Gene expression profiling of mantle cell lymphoma and its blastoid variant.

AUTHOR: Zhu Y(a); Hollmen J; Oinonen R; Franssila K; Aalto Y(a); Elonen E; Manninen H; Kere J(a); Knuutila S(a)

AUTHOR ADDRESS: (a)Medical Genetics, Haartman Institute and Helsinki University Central Hospital, Helsinki**Finland

JOURNAL: European Journal of Cancer 37 (Supplement 6):pS41 October, 2001

MEDIUM: print

CONFERENCE/MEETING: 11th European Cancer Conference Lisbon, Portugal October 21-25, 2001

ISSN: 0959-8049

RECORD TYPE: Citation

LANGUAGE: English

DESCRIPTORS:

MAJOR CONCEPTS: **Tumor** Biology

BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGANISMS: human (Hominidae)--patient

BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Chordates; Humans; Mammals; Primates; Vertebrates

DISEASES: mantle cell lymphoma--blood and lymphatic disease, **neoplastic** disease

CHEMICALS & BIOCHEMICALS: Annexin II; CD44; CD66d; bcl2; **granulin precursor**; regulator of G protein signaling 1 {RGS1}; regulator of G protein signaling 2 {RGS2}

GENE NAME: ADA gene; AF-17 gene; EB12 gene; GPR13 gene; c-myc oncogene

METHODS & EQUIPMENT: Atlas Human Hematology array filter--laboratory equipment; AtlasImage software--computer software; European-American classification of lymphoid **neoplasms**--classification method; cDNA micro-array analysis {complementary DNA micro-array analysis}--analytical method, detection method; cDNA micro-array experiment {complementary DNA micro-array experiment}--detection method, molecular genetic method; gene expression profiling--detection method, molecular genetic method; principal component analysis--analytical method, mathematical method; regression analysis--analytical method, mathematical method

8/9/2 (Item 2 from file: 5)

DIALOG(R)File 5: Biosis Previews(R)

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13611262 BIOSIS NO.: 200200240083

Expression of progranulin and the epithelin/ granulin precursor acrogranin correlates with neoplastic state in renal epithelium.

AUTHOR: Donald Carlton D; Laddu Abhay; Chandham Priti; Lim So Dug; Cohen Cynthia; Amin Mahul; Gerton George L; Marshall Fray F; Petros John A(a)

AUTHOR ADDRESS: (a)Department of Urology, Emory University, 1365-B Clifton Road, Rm. 4222, Atlanta, GA, 30322**USA

JOURNAL: Anticancer Research 21 (6A):p3739-3742 November-December, 2001

MEDIUM: print

ISSN: 0250-7005

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: Background: Current traditional pathological parameters, including staging and grading, are not sufficient in predicting outcome

in patients with renal cell carcinoma (RCC). Acrogranin is an epithelial growth factor and has been demonstrated to play a role in teratocarcinogenesis and **tumorigenesis**. The aim of this study was to examine levels of acrogranin in renal **cancer**. Materials and Methods: Western blot analysis was performed on renal tissue protein lysates. In addition, immunohistochemical (IHC) analysis of acrogranin expression was conducted on tissue sections of various histological types and grades of RCC. Results: Western analysis showed that acrogranin levels were low in benign renal tissue and increased in malignant renal tissue. In addition, IHC revealed that high-grade RCC exhibited higher levels of expression than low-grade RCC and normal tissue. Conclusion: These data suggest that acrogranin may be a functionally important growth factor in RCC and may be a potential molecular marker for high-grade RCC.

8/9/3 (Item 3 from file: 5)
DIALOG(R)File 5:BIOSIS Previews(R)
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13372875 BIOSIS NO.: 200200001696

PC-cell derived growth factor (PCDG, progranulin) expression and action in human multiple myelomas.

AUTHOR: Wang Wengang(a); Hayashi Jun(a); You Jun(a); Serrero Ginette(a)
AUTHOR ADDRESS: (a)University of Maryland School of Pharmacy, Baltimore, MD
**USA

JOURNAL: Proceedings of the American Association for Cancer Research Annual Meeting 42p835 March, 2001

MEDIUM: print

CONFERENCE/MEETING: 92nd Annual Meeting of the American Association for Cancer Research New Orleans, LA, USA March 24-28, 2001

ISSN: 0197-016X

RECORD TYPE: Citation

LANGUAGE: English

REGISTRY NUMBERS: 139316-59-9: PROGRANULIN; 50-02-2: DEXAMETHASONE

DESCRIPTORS:

MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; **Tumor** Biology
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGANISMS: ARP-1 cell line (Hominidae)--human multiple myeloma cells;
RPMI 8226 cell line (Hominidae)--human multiple myeloma cells; human (Hominidae)--patient

ORGANISMS: PARTS ETC: bone marrow--blood and lymphatics, immune system

BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Chordates; Humans; Mammals; Primates; Vertebrates

DISEASES: multiple myeloma {MM}--blood and lymphatic disease, immune system disease, **neoplastic** disease

CHEMICALS & BIOCHEMICALS: PC-cell derived growth factor { **PCDGF** , progranulin}--expression; dexamethasone--antineoplastic-drug; interleukin-6; mRNA {messenger RNA

METHODS & EQUIPMENT: Northern blot--blotting/hybridization/molecular probe techniques, detection method, labeling; Western blot--detection method, gene mapping, labeling; immunocytochemistry--immunological method

MISCELLANEOUS TERMS: **tumorigenicity** ; Meeting Abstract

8/9/4 (Item 4 from file: 5)
DIALOG(R)File 5:BIOSIS Previews(R)
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12896283 BIOSIS NO.: 200100103432

Mediation of estrogen mitogenic effect in human breast cancer MCF-7 cells by PC-cell-derived growth factor (PCDGF / granulin precursor).

AUTHOR: Lu Runqing; Serrero Ginette(a)

AUTHOR ADDRESS: (a)Department of Pharmaceutical Sciences, University of Maryland School of Pharmacy, 20 North Pine Street, Baltimore, MD, 21201-1180: gserrero@rx.umaryland.edu**USA

JOURNAL: Proceedings of the National Academy of Sciences of the United States of America 98 (1):p142-147 January 2, 2001

MEDIUM: print

ISSN: 0027-8424

DOCUMENT TYPE: Article

RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: PC-cell-derived growth factor (**PCDGF**) is an 88-kDa glycoprotein corresponding to the **granulin precursor** . We have reported that **PCDGF** was expressed in human breast **cancer** cells. In estrogen-receptor positive cells, 17-beta-estradiol (E2) transcriptionally stimulated **PCDGF** expression in a dose- and time-dependent fashion. We demonstrate here that **PCDGF** mediates the mitogenic effect of E2 in MCF-7 cells. **PCDGF** substituted for E2 to stimulate DNA synthesis. The E2 mitogenic effect was inhibited in a dose-dependent fashion by anti- **PCDGF** neutralizing antibody. Inhibition of **PCDGF** expression by antisense transfection also inhibited the E2 mitogenic effect. In contrast, overexpression of **PCDGF** in MCF-7 cells resulted in cells that were able to proliferate in the absence of estrogen and were tamoxifen resistant. The **PCDGF** signaling pathway was examined. Like E2, **PCDGF** stimulated mitogen-activated protein kinase activity. **PCDGF** could substitute for E2 in stimulating cyclin D1 expression. The cyclin D1 stimulation by E2 was 50% inhibited by anti- **PCDGF** antibody. In contrast, **PCDGF** did not stimulate c-myc expression, another molecular target of E2. We conclude that autocrine **PCDGF** mediates the E2 mitogenic effect via stimulation of cyclin D1. These studies provide information on estrogen action and identify an autocrine molecular target in human breast **cancer** cells.

8/9/5 (Item 5 from file: 5)
DIALOG(R)File 5: Biosis Previews(R)
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12590324 BIOSIS NO.: 200000343826

Autocrine growth factor and estrogen-independence in human breast cancer cells.

AUTHOR: Serrero G(a); Lu R(a); You J(a)
AUTHOR ADDRESS: (a)Dept. Pharmaceutical Sciences, University of Maryland School of Pharmacy, Baltimore, MD, 21201**USA
JOURNAL: In Vitro Cellular & Developmental Biology Animal 36 (3 Part 2):p 27A March, 2000
MEDIUM: print
CONFERENCE/MEETING: Meeting of the Society for In Vitro Biology World Congress on In Vitro Biology San Diego, California, USA June 10-15, 2000
ISSN: 1071-2690
RECORD TYPE: Citation
LANGUAGE: English
SUMMARY LANGUAGE: English
REGISTRY NUMBERS: 50-28-2: ESTRADIOL; 10540-29-1: TAMOXIFEN
DESCRIPTORS:

MAJOR CONCEPTS: Reproductive System (Reproduction); **Tumor** Biology
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: human (Hominidae)
ORGANISMS: PARTS ETC: estrogen receptor positive cell--mitogenesis
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Chordates; Humans; Mammals; Primates; Vertebrates
DISEASES: breast **cancer** -- **neoplastic** disease, reproductive system disease/female, **tumor** formation
CHEMICALS & BIOCHEMICALS: PC-Cell Derived Growth Factor { **PCDGF** }--expression; estradiol; estrogen--independence; tamoxifen
MISCELLANEOUS TERMS: Meeting Abstract

8/9/6 (Item 6 from file: 5)
DIALOG(R)File 5: Biosis Previews(R)
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12498700 BIOSIS NO.: 200000252202

Inhibition of PC cell-derived growth factor (**PCDGF , **epithelin/ granulin precursor**) expression by antisense **PCDGF** cDNA transfection inhibits tumorigenicity of the human breast carcinoma cell line MDA-MB-468.**

AUTHOR: Lu Runqing; Serrero Ginette(a)
AUTHOR ADDRESS: (a)Department of Pharmaceutical Sciences, University of Maryland School of Pharmacy, 20 North Pine Street, Baltimore, MD, 21201-1180**USA

JOURNAL: Proceedings of the National Academy of Sciences of the United States of America 97 (8):p3993-3998 April 11, 2000

ISSN: 0027-8424

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

ABSTRACT: PC-cell derived growth factor (**PCDGF**) is an 88-kDa growth factor originally purified from the highly **tumorigenic** teratoma PC cell line and corresponds to the epithelin/ **granulin precursor** . In teratoma cells, **PCDGF** expression was shown to be essential for **tumorigenicity** . We have reported that **PCDGF** was expressed in estrogen receptor-positive (ER+) human mammary epithelial cells in an estrogen-dependent fashion. In this study, we have investigated **PCDGF** expression in human mammary epithelial cell lines ranging from immortalized nontumorigenic cells to ER+ and ER- breast carcinoma cells. Northern and Western blot analyses indicated that **PCDGF** mRNA and protein expression was low in nontumorigenic cells and increased in human breast carcinomas cell lines in a positive correlation with their **tumorigenicity** . Treatment of the ER- MDA-MB-468 cells with anti- **PCDGF** neutralizing antibody resulted in a dose-dependent inhibition of their proliferation, suggesting that secreted **PCDGF** acted as an autocrine growth factor for breast carcinoma cells. We then examined the in vitro and in vivo growth properties of MDA-MB-468 cells, where **PCDGF** expression had been inhibited by antisense **PCDGF** cDNA transfection. Inhibition of **PCDGF** expression resulted in a reduced proliferation rate in vitro and a 60-80% reduction in colony formation. **Tumor** formation in vivo was dramatically inhibited in antisense cells with a 90% inhibition of **tumor** incidence and **tumor** weight. These results demonstrate the importance of **PCDGF** overexpression for the proliferation and **tumorigenicity** of ER- breast carcinomas and suggest that **PCDGF** overexpression may play an important role in human breast **cancer** .

8/9/7 (Item 7 from file: 5)

DIALOG(R) File 5: Biosis Previews(R)

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11761797 BIOSIS NO.: 199900007906

Inhibition of tumorigenicity of the teratoma PC cell line by transfection with antisense cDNA for PC cell-derived growth factor (PCDGF , epithelin/ granulin precursor).

AUTHOR: Zhang Haidi; Serrero Ginette(a)

AUTHOR ADDRESS: (a)Dep. Pharmaceutical Sci., Univ. Md., Sch. Pharm., 20 North Pine St., Baltimore, MD 21201-1180**USA

JOURNAL: Proceedings of the National Academy of Sciences of the United States of America 95 (24):p14202-14207 Nov. 24, 1998

ISSN: 0027-8424

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: The PC cell line is a highly **tumorigenic** , insulin-independent, teratoma-derived cell line isolated from the nontumorigenic, insulin-dependent 1246 cell line. Studies of the PC cell growth properties have led to the purification of an 88-kDa secreted glycoprotein called PC cell-derived growth factor (**PCDGF**), which has been shown to stimulate the growth of PC cells as well as 3T3 fibroblasts. Sequencing of **PCDGF** cDNA demonstrated its identity to the precursor of a family of 6-kDa double-cysteine-rich polypeptides called epithelins or granulins (epithelin/ **granulin precursor**). Since **PCDGF** was isolated from highly **tumorigenic** cells, its level of expression was examined in PC cells as well as in nontumorigenic and moderately **tumorigenic** cells from which PC cells were derived. Northern blot and Western blot analyses indicate that the levels of **PCDGF** mRNA and protein were very low in the nontumorigenic cells and increased in **tumorigenic** cell lines in a positive correlation with their **tumorigenic** properties. Experiments were performed to determine whether the autocrine production of **PCDGF** was involved in the **tumorigenicity** of PC cells. For this purpose, we examined the in vivo growth properties

in syngeneic C3H mice of PC cells where **PCDGF** expression had been inhibited by transfection of antisense **PCDGF** cDNA. The results show that inhibition of **PCDGF** expression resulted in a dramatic inhibition of **tumorigenicity** of the transfected cells when compared with empty-vector control cells. These data demonstrate the importance in **tumor** formation of overexpression of the novel growth factor **PCDGF**.

8/9/8 (Item 8 from file: 5)
DIALOG(R)File 5: Biosis Previews(R)
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11472403 BIOSIS NO.: 199800253735

Identification of cell surface binding sites for PC-cell-derived growth factor, PCDGF, (epithelin/ granulin precursor) on epithelial cells and fibroblasts.

AUTHOR: Xia Xianmin; Serrero Ginette(a)
AUTHOR ADDRESS: (a)Dep. Pharm. Sci., Univ. Maryland Sch. Pharm., Univ. Maryland, 20 North Pine Street, Baltimore, M**USA
JOURNAL: Biochemical and Biophysical Research Communications 245 (2):p 539-543 April 17, 1998
ISSN: 0006-291X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: PC cell derived growth factor (**PCDGF**) is an 88-kDa glycoprotein purified from the culture medium of the highly **tumorigenic** mouse teratoma-derived cell line PC. **PCDGF** was shown to stimulate the proliferation of 3T3 fibroblasts and PC cells. Amino acid sequencing of **PCDGF** indicated its identity to the precursor for the 6-kDa polypeptides epithelins and granulins. In this paper, we investigated the binding of **PCDGF** to the mink lung epithelial cell line CCL64. Scatchard analysis indicates that 125I- **PCDGF** binding to CCL64 cells is curvilinear, corresponding to the existence of two classes of binding sites: high affinity binding sites (560 +/- 170 sites/cell) with a Kd1 of 43+-15 pM and low affinity binding sites (16,350 +/- 5900 sites/cell) with a Kd2 of 3.9 +/- 1.9 nM. 125I- **PCDGF** was chemically crosslinked to cell surface receptors on CCL64 cells with disuccinimidyl suberate. A major crosslinked band of about 190 kDa with radiolabeled **PCDGF** was detected after SDS-PAGE, suggesting the presence of **PCDGF** binding sites with molecular weight of about 120 kDa. 125I- **PCDGF** crosslinking studies indicate the presence of **PCDGF** binding sites with a molecular weight similar to those of binding sites on CCL64 cells on the surface of two other **PCDGF**-responsive cell lines, 3T3 fibroblasts and PC cells. These data suggest that the receptors for **PCDGF** are widely distributed on cells of distinct embryonic origin.

8/9/10 (Item 10 from file: 5)
DIALOG(R)File 5: Biosis Previews(R)
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08890139 BIOSIS NO.: 199396041640

Purification of an autocrine growth factor homologous with mouse epithelin precursor from a highly tumorigenic cell line.

AUTHOR: Zhou Jian; Gao Guan; Crabb John W; Serrero Ginette(a)
AUTHOR ADDRESS: (a)W. Alton Jones Cell Sci. Center, Inc., Lake Placid, NY 12946**USA
JOURNAL: Journal of Biological Chemistry 268 (15):p10863-10869 1993
ISSN: 0021-9258
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: PC cell line is a highly **tumorigenic** insulin-independent variant from the teratoma-derived adipogenic cell line 1246. Culture medium of PC cells contains a growth promoting activity for 3T3 cells and producer cells. PC cell-derived growth factor (**PCDGF**) was purified to homogeneity from PC cell-conditioned medium as an apparent 88-kDa protein by chromatography on heparin-Sepharose, Sephacryl S-200, and phenyl-Sepharose. Digestion with peptide-N-glycosidase F yielded an

apparent 68-kDa protein component indicating that **PCDGF** is a glycoprotein containing about 20 kDa of carbohydrate. Partial sequence from Edman degradation of peptide fragments obtained by digestion of **PCDGF** with cyanogen bromide and trypsin demonstrates that **PCDGF** contains regions of sequence identity to that deduced from the granulin or epithelin precursor cDNAs. Granulins are small polypeptides purified from granulocyte extracts with no apparent biological functions. Epithelins are cell growth modulators purified as small molecular mass 6-kDa polypeptides from kidney extracts. The existence of a large molecular mass precursor for granulin or epithelin has been predicted based upon recently cloned cDNAs encoding these biomolecules within a 63.5-kDa protein with putative glycosylation sites. No biological activity has previously been attributed to the precursor. The present results indicate that **PCDGF** is a potential precursor for epithelin and/or granulin, that this 88-kDa protein is secreted and glycosylated, and that it can function as a mitogen for 3T3 cells as well as an autocrine growth factor for PC cells.

8/9/11 (Item 1 from file: 155)

DIALOG(R) File 155: MEDLINE(R)

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10194461 99167362 PMID: 10066447

Stimulation of PC cell-derived growth factor (epithelin/ granulin precursor) expression by estradiol in human breast cancer cells.

Lu R; Serrero G

Department of Pharmaceutical Sciences, University of Maryland School of Pharmacy, 20 North Pine Street, Baltimore, Maryland, 21201, USA.

Biochemical and biophysical research communications (UNITED STATES) Mar 5 1999, 256 (1) p204-7, ISSN 0006-291X Journal Code: 0372516

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

PC cell-derived growth factor (**PCDGF**) is an 88 kDa glycosylated protein isolated from a highly **tumorigenic** mouse teratoma derived cell line which is similar to the epithelin/ **granulin precursor** . Using Northern blot and western blot analyses, we detect the expression of **PCDGF** mRNA and protein in MCF-7 human breast **cancer** cells. We show that 17-beta-estradiol stimulates **PCDGF** mRNA and protein expression in a time and dose-dependent manner. The stimulation of **PCDGF** expression by 17-beta-estradiol was observed as early as 4 hours and reached a maximum at 12 hours. Maximal stimulation of **PCDGF** mRNA and protein expression by 17-beta-estradiol was observed at a concentration of 10(-8) M. The stimulation of **PCDGF** expression by 17-beta-estradiol was completely inhibited by treatment with actinomycin D and with the antiestrogen 4-hydroxytamoxifen. The stimulation of **PCDGF** expression was also demonstrated in another human estrogen-responsive cell line T47D. The results presented here provide evidence of a novel estradiol responsive gene product in human breast **cancer** cell lines and give information about the hormonal control of epithelin/granulin (**PCDGF**) expression in these cells. Copyright 1999 Academic Press.

8/9/13 (Item 2 from file: 34)

DIALOG(R) File 34: SciSearch(R) Cited Ref Sci

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07822741 Genuine Article#: 212BL Number of References: 33

Title: Progranulin gene expression regulates epithelial cell growth and promotes tumor growth in vivo

Author(s): He ZH; Bateman A (REPRINT)

Corporate Source: MCGILL UNIV, ENDOCRINE LAB, ROYAL VICTORIA HOSP, DEPT MED, ROOM L2-05, 687 PINE AVE W/MONTREAL/PQ H3A 1A1/CANADA/ (REPRINT); MCGILL UNIV, ENDOCRINE LAB, ROYAL VICTORIA HOSP, DEPT MED/MONTREAL/PQ H3A 1A1/CANADA/

Journal: CANCER RESEARCH, 1999, V59, N13 (JUL 1), P3222-3229

ISSN: 0008-5472 Publication date: 19990701

Publisher: AMER ASSOC CANCER RESEARCH, PO BOX 11806, BIRMINGHAM, AL 35202

Language: English Document Type: ARTICLE

Geographic Location: CANADA

Subfile: CC LIFE--Current Contents, Life Sciences; CC CLIN--Current
Contents, Clinical Medicine

Journal Subject Category: ONCOLOGY

Abstract: Progranulin is a 593-amino acid glycoprotein, the mRNA of which is expressed by many epithelial cells both in vitro and ill vivo, but the biological significance of this expression is unclear. In this study, we demonstrate that overexpression of the progranulin gene in SW-13 adrenal carcinoma cells and MDCK nontransformed renal epithelia results in the transfection-specific secretion of progranulin, acquired clonogenicity in semisolid agar, and increased mitosis in monolayer culture, whereas diminution of progranulin gene expression impairs growth of these cells. purified recombinant progranulin reproduces the effects of forced progranulin expression, being clonogenic in soft agar and mitogenic in monolayer culture to SW-13 and MDCK cells and other epithelia of various origins such as GPC16 colonic epithelium and A549 lung carcinoma cells. Progranulin overproduction in SW-13 cells markedly increases its **tumor** -genicity in nude mice, demonstrating that it can regulate epithelial proliferation ill vivo. We propose that the rate of growth for some epithelia, such as SW-13 and MDCK, is proportional to the level of intrinsic progranulin gene expression, and that elevated progranulin gene expression confers a transformed phenotype on epithelial cells including anchorage independence in vitro and growth as **tumors** in nude mice.